

8EHQ-0403-152113

U.S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

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March 18, 2003

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SANITIZED – NON-CBI

TSCA Document Processing Center
U. S. Environmental Protection Agency
Office of Pollution Prevention and Toxics (7407M)
EPA East Building, Room 6428
1200 Pennsylvania Ave., NW
Washington, DC 20460

MANDATORY SANITIZED

Attention: TSCA 8(e) Submittal



REFERENCE: 8EHQ-02-15211

[] is submitting this supplemental information pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA). This submission supplements an earlier submission (8EHQ-02-15211) for []

[] This material has been tested under the name []

A modified female rat pubertal assay and a male rat Hershberger assay were conducted with a []

In the Hershberger assay, castrated male rats (N = 10/group) received ten daily doses of 0 (vehicle, corn oil, 5 mL/kg), 150, or 500 mg/kg/day of [] by oral gavage, beginning at 50 days of age. Half of the groups also received a daily subcutaneous injection of testosterone propionate (0.4 mg/kg/day). Daily body weights were recorded. At 60 days of age, all males were euthanized, and weights of the following were recorded: liver, Cowper's gland, glans penis, levator ani/bulbocavernosus muscles, seminal vesicles with coagulating glands, and ventral prostate.

In the female pubertal assay, female rats 22 days of age (N = 15/group) received 20 daily doses of [] at levels of 0 (vehicle, corn oil, 5 mL/kg), 50, 150, and 500 mg/kg/day by oral gavage. Daily body weights were recorded. Beginning at 25



265640

3/18/2003

Page 2

days of age, each female was observed daily for vaginal perforation. Vaginal smears for determination of estrus were performed daily upon the completion of vaginal perforation. At 42 days of age, all females were euthanized, and weights of the following were recorded: liver, ovaries, wet and blotted uterus, pituitary gland, adrenal glands.

Unaudited draft results for each of the assays are attached. In the male assay, co-administration of [] at 500 mg/kg/day with testosterone propionate resulted in a decrease in the weight of the seminal vesicles/coagulating glands. Liver weights were significantly increased in this group as well. In the female assay, administration of 500 mg/kg/day of [] resulted in an apparent acceleration of vaginal perforation, a decrease in uterine blotted and wet weights, decreased weight of the combined ovaries, and increased liver weight.

Additional male and female assays will be conducted with [].
When all such assays are completed, we will report any further positive findings.

We consider this letter to be "Confidential Business Information" (CBI); therefore, we are also enclosing a "sanitized" (non-CBI) version and CBI Substantiation Questions.

If you have any questions, please contact me at [].

Sincerely,

Signature removed

[]
[]

Attachments (2)

PROJECT NO. .
SPONSOR
SPONSOR NO. :

HERSHBERGER ASSAY

SUMMARY OF ORGAN WEIGHTS (G)

ON MALE RATS

13:39 26-FEB-03 PAGE 1
DAY 10

GROUP:	M A L E				
	0/0 MG/KG	150/0 MG/KG	500/0 MG/KG	0/0.4 MG/KG	150/0.4 MG/KG
LIVER (G)					
MEAN	13.32	14.14	15.17	14.05	15.10
S.D.	1.136	1.050	2.158	1.321	1.893
N	10	10	10	10	10
SPM VES/COAG GL (G)					
MEAN	0.0898	0.0822	0.1003	0.0850b	0.0756cb
S.D.	0.03014	0.02081	0.01997	0.10953	0.13542
N	10	10	10	10	10
VENTRAL PROSTATE (G)					
MEAN	0.0351	0.0291	0.0281	0.02199b	0.02400b
S.D.	0.01669	0.01096	0.01240	0.04356	0.04854
N	10	10	10	10	10
LABC MUSCLE CR. (G)					
MEAN	0.1925	0.1936	0.1851	0.5502b	0.5174b
S.D.	0.03421	0.01978	0.03382	0.06249	0.11354
N	10	10	10	10	10
STOMACH PERIT. (G)					
MEAN	0.0626	0.0898	0.0790	0.1083b	0.1120b
S.D.	0.01262	0.02121	0.01401	0.01453	0.03194
N	10	10	10	10	10

MODIFIED STATISTICAL TESTS : INDICATES SIGNIFICANT DIFF. : INDICATES NO SIGNIFICANT DIFFERENCES.

For statistical analysis, control group 1 was compared to groups 2, 3, 4, 5 and 6. Control group 6 was compared to group 5.

Control group 4 was compared to group 5.

b = significantly different from control group 1 at 0.01 using Dunnett's test.

c = significantly different from control group 4 at 0.05 using Dunnett's test.

1 = significantly different from control group 1 at 0.01 using Dunnett's test.

11:39 26-FEB-03 PAGE 2
DAY 10

IN MME RATS

SUMMARY OF ORGAN WEIGHTS (G)

RECHENBERGER ASSAY

PROJECT NO.
SPONSOR
SPONSOR NO.

GROUP:	M A L E			
	0/0 MG/KG	150/0 MG/KG	0/0.4 MG/KG	150/0.4 MG/KG
REPOURTRIAL OL (G)				
MEAN	0.0087	0.0059	0.0079	0.0076
S.D.	0.00203	0.00215	0.00164	0.00155
N	10	10	10	10

MODIFIED STATISTICS USED. * INDICATES PARAMETRIC ANALYSIS AND + INDICATES NON-PARAMETRIC ANALYSIS.

For statistical analyses, control group 1 was compared to groups 2, 3, 4, 5 and 6, control group 4 was compared to group 5; control group 4 was compared to group 6.

b = Significantly different from control group 1 at 0.01 using Dunnett's test

POWER5.02
02/26/2003

PRODUCT NO.
SPONSOR
SPONSOR NO.

HERSHBERGER ASSAY SUMMARY OF ORGANS WTS. RELATIVE TO FINAL BODY WTS. (G/100 G)

IN PALE RATS

13-40 26-FEB-03 PAGE 1
DAY 10

GROUP	M A L E				
	0/0 MG/KG	150/0 MG/KG	500/0 MG/KG	0/0.4 MG/KG	150/0.4 MG/KG
FINAL BODY WT (G)					
MEAN	316.	313.	296.	327.	334.
S.D.	31.4	26.0	28.5	26.3	29.9
N	10	10	10	10	10
LIVER					
MEAN	4.227	4.529	5.125b	4.389	4.521
S.D.	0.2453	0.2185	0.6102	0.2346	0.3790
N	10	10	10	10	10
SEM VES/CONS GL					
MEAN	0.028	0.026	0.034	0.212b	0.228b
S.D.	0.0092	0.0071	0.0075	0.0275	0.0406
N	10	10	10	10	10
VESICULAR PROSTATE					
MEAN	0.011	0.005	0.009	0.066b	0.072b
S.D.	0.0052	0.0034	0.0037	0.0140	0.0148
N	10	10	10	10	10
LARGE NODULES OR					
MEAN	0.001	0.002	0.001	0.169b	0.165b
S.D.	0.0077	0.0056	0.0054	0.0170	0.0294
N	10	10	10	10	10

STATISTICAL ANALYSIS: * INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.05 USING PARAMETRIC ANALYSIS.
* INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.01 USING NON-PARAMETRIC ANALYSIS.
* INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.05 USING PARAMETRIC ANALYSIS.
* INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.01 USING NON-PARAMETRIC ANALYSIS.
* INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.05 USING PARAMETRIC ANALYSIS.
* INDICATES SIGNIFICANT DIFFERENCE FROM CONTROL GROUP 0.01 USING NON-PARAMETRIC ANALYSIS.

GROUP:	0/G MG/KG	150/0 MG/KG	500/0 MG/KG	0/0.4 MG/KG	150/0.4 MG/KG	500/0.4 MG/KG
BLADDER PENIS						
MEAN	0.025	0.029	0.027	0.050b	0.046b	0.047b
S.D.	0.0041	0.0053	0.0049	0.0060	0.0056	0.0061
N	10	10	10	10	10	10
SUBROUTINE: GL						
MEAN	0.003	0.002	0.002	0.012b	0.012b	0.011b
S.D.	0.0006	0.0008	0.0005	0.0016	0.0025	0.0016
N	10	10	10	10	10	10

MODIFIED STATISTICS USED. * INDICATES PARAMETRIC ANALYSIS AND + INDICATES NON-PARAMETRIC ANALYSIS.
 For statistical analyses, control group 1 was compared to groups 2, 3, 4, 5 and 6; control group 4 was compared to group 5;
 control group 4 was compared to group 6.
 b = Significantly different from control group 1 at 0.01 using Dunnett's test

POB52V5.02
 02/26/2002

PROJECT NO.
 C-70000
 GIBSON HO-1

UNAUDITED DRAFT
 GENERAL ASSAY OF
 SUMMARY OF ANIMAL DEVELOPMENTAL PARAMETERS

14.30 6-MDP-03 PAGE 1

GROUP 1 2 3 4
 FEMALES
 VAGINAL EPITHELIUM

VAGINAL EPITHELIUM (mm)
 MEAN 31.1 25.1 33.5 33.2
 S.D. 1.67 1.25 1.25 1.92
 N 15 15 15 15

BODY WEIGHT
 MEAN 115.4 123.6 110.3 103.9
 S.D. 11.13 13.85 10.09 9.69
 N 15 15 15 15

PRINTED
 03/06/2003

PROJECT NO.
S. NUMBER
CONTAINER NO.

STUDY AREA

UNADULTED DRAFT

SUMMARY OF GREGG'S RESULTS

1974 JAN-01 2000
DAY 20

GROUP	0-100% / DAY	0-100% / DAY	0-100% / DAY	0-100% / DAY
UNADULTED MEET (G)				
MEAN	0.4400	0.4400	0.4400	0.4400
S.D.	0.1793	0.1793	0.1793	0.1793
N	15	15	15	15
UNADULTED PLANT (G)				
MEAN	0.3610	0.3610	0.3610	0.3610
S.D.	0.07963	0.07963	0.07963	0.07963
N	15	15	15	15
UNADULTED (G)				
MEAN	7.16	7.93	7.93	8.49**
S.D.	0.671	1.177	1.545	1.065
N	15	15	15	15
OVERLIES (G)				
MEAN	0.0958	0.0958	0.0958	0.0958
S.D.	0.07102	0.07102	0.07102	0.07102
N	15	15	15	15
UNADULTED PLANT (G)				
MEAN	0.0039	0.0039	0.0039	0.0039
S.D.	0.0000	0.0000	0.0000	0.0000
N	15	15	15	15

* Significantly different from the control group at 0.01 using Dunn-Sidak test

PROJECT NO.
CONTRACT
APPROVAL NO.

PIPERAL ASSEY

INHALED QUANT

STANDARD OF GROSS WEIGHTS (G)

14:24 11-JAN 02 1400
DAY 25

STATION	66/50/70/1	P & M A L E	100 M/50/70/1	500 M/50/70/1
MSBN	0.0022	0.0024	0.0025	0.0026
S.D.	0.00112	0.00112	0.00112	0.00112
N	15	15	11	14

None significantly different from control group

FOURSTV4.02
02/11/2003

PROJECT NO.
SPECIMEN NO.

PURPOSE, ACCOUNT OF
SUBJECT OF ORIGIN WITH REFERENCE TO FINAL BODY SITE, NO/100 CI

14/11/11 11:00 AM 01 JANUARY 1971

GROUP	0.00/100/100	0.00/100/100	0.00/100/100	0.00/100/100
EMBRYO BODY AT (G)				
MEAN	112	112	112	112
S.D.	2.9	2.9	2.9	2.9
N	15	15	12	13
DIFFUSION MEAN				
MEAN	0.286	0.213	0.261	0.292
S.D.	0.1097	0.0979	0.1556	0.0969
N	15	15	11	19
UTERUS MEAN				
MEAN	0.237	0.189*	0.213	0.165**
S.D.	0.0467	0.0663	0.0645	0.0412
N	15	15	13	14
LIVER MEAN				
MEAN	4.704	4.663	5.013	5.585**
S.D.	0.4835	0.4856	0.5536	0.4874
N	15	15	13	14
SPLEEN MEAN				
MEAN	0.077	0.077	0.077*	0.077**
S.D.	0.013	0.0061	0.0093	0.0091
N	15	15	13	19

* Significantly different from the control group at 0.05 using Dunnett's test.
** Significantly different from the control group at 0.01 using Dunnett's test.

PROJECT NO.
SPONSOR NO.

UNAUDITED DATA
SUBJECT OF CHRON WTS. RELATIVE TO HIND. BODY WTS. (g/100 g)

10-24 11-24 12-24 13-24 14-24 15-24 16-24 17-24 18-24 19-24 20-24 21-24 22-24 23-24 24-24 25-24 26-24 27-24 28-24 29-24 30-24 31-24 32-24 33-24 34-24 35-24 36-24 37-24 38-24 39-24 40-24 41-24 42-24 43-24 44-24 45-24 46-24 47-24 48-24 49-24 50-24 51-24 52-24 53-24 54-24 55-24 56-24 57-24 58-24 59-24 60-24 61-24 62-24 63-24 64-24 65-24 66-24 67-24 68-24 69-24 70-24 71-24 72-24 73-24 74-24 75-24 76-24 77-24 78-24 79-24 80-24 81-24 82-24 83-24 84-24 85-24 86-24 87-24 88-24 89-24 90-24 91-24 92-24 93-24 94-24 95-24 96-24 97-24 98-24 99-24 100-24

10-24 11-24 12-24 13-24 14-24 15-24 16-24 17-24 18-24 19-24 20-24 21-24 22-24 23-24 24-24 25-24 26-24 27-24 28-24 29-24 30-24 31-24 32-24 33-24 34-24 35-24 36-24 37-24 38-24 39-24 40-24 41-24 42-24 43-24 44-24 45-24 46-24 47-24 48-24 49-24 50-24 51-24 52-24 53-24 54-24 55-24 56-24 57-24 58-24 59-24 60-24 61-24 62-24 63-24 64-24 65-24 66-24 67-24 68-24 69-24 70-24 71-24 72-24 73-24 74-24 75-24 76-24 77-24 78-24 79-24 80-24 81-24 82-24 83-24 84-24 85-24 86-24 87-24 88-24 89-24 90-24 91-24 92-24 93-24 94-24 95-24 96-24 97-24 98-24 99-24 100-24

GROUP	0 W/100/DAY	50 W/100/DAY	150 W/100/DAY	250 W/100/DAY
ABNORMAL CLAMPS				
MEAN	0.026	0.026	0.027	0.026
S.D.	0.0039	0.0029	0.0049	0.0037
N	15	15	11	14
PRIMARY				
MEAN	0.005	0.005	0.005	0.005
S.D.	0.0009	0.0008	0.0005	0.0007
N	15	15	12	14

None significantly different from control group

FOREFGINS.02
03/11/2003